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EXAMINER	
MOORE, WILLIAM W	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 10/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/830,837	SEIDAH ET AL.	
	Examiner	Art Unit	
	William W. Moore	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *30,31,36,37,40-44,72,73,80-83,92,98,104 and 114* is/are allowed.

6)☒ Claim(s) *32,45-49,51,52,54,55,59,60,65,67,93-97,99-103,105-109 and 115-119* is/are rejected.

7)☒ Claim(s) *53 and 56* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20011018*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 28 July 2005 has been entered.

Priority

Applicant's claim to the priority of the filing date of the International Application, PCT/CA99/01058 filed 4 November 1999, and the further claim to priority under 35 U.S.C. § 119 of the Canadian patent application No. 2,249,648 filed 4 November 1998 were acknowledged on the cover page of the communication mailed 12 February 2003.

The Article 34 Amendment in the parent PCT application presented the originally filed claims in this application that define, see, e.g., claims 1 and 17, a "SKI-1 soluble fragment", as having the amino acid sequence of "amino acids 187 to **996**" of e.g., SEQ ID NO:6, thus the subject matters of claims 30, 36, 40-45, 65, 72, and 80-83 herein have an adequate written description in the claims filed on 1 May 2001 which are a part of the disclosure of the specification. In addition, the Amendment filed 22 December 2003 amended claim 31 to correct the erroneous assignment of cysteine as the 17th amino acid of a precursor SKI-1 convertase at page 38, line 8, of the specification by changing the initial amino acid of the polypeptide from position 18 to position 17 of SEQ ID NO:6. This correction is both appropriate and necessary because SEQ ID NO:6 sets forth cysteine as the 16th amino acid and the adjacent glycine as the 17th amino acid, thus the specification inherently discloses that the amino acid sequence of a SKI-1 polypeptide begins with glycine at position 17 upon cleavage of the signal peptide within

a host cell and extends through position 137 of SEQ ID NO:6. This is considered to be an inherent disclosure as well of an isolated polynucleotide of claim 37 encoding the polypeptide and compositions of claims 67 and 73 comprising either the polypeptide of claim 31 or a polynucleotide of claim 37. Similarly, the terminal clause of claim 31 appropriately describes a binding partner of the polypeptide of lines 1-3 of the claim in stating, lines 4-5, "amino acids **17** to 1052 of SKI-1" because the amino terminus of an SKI-1 convertase processed by a signal peptidase within a host cell will be the amino acid at position 17 in the sequence of SEQ ID NO:6. The Amendment of 22 December 2003 also corrects an erroneous assignment at pages 32 and 36 of the specification of position **997** as the carboxyl terminus of a soluble SKI-1 convertase by reciting instead "996" in claims 30, 46, 47.

Amendment

The amendments to claims 30, 31, 46, 47, 51-53, 55, 56, 59, 60, 65, 67 and 92-109 filed 28 July 2005, together with cancellations of claims 38, 66, 68 and 74, overcome the objections of record of claims herein under 37 CFR 1.75 and for informalities, and overcome as well the rejections of record of claims 46-49, 51-55, 59 and 60 under 35 U.S.C. §112, first paragraph, and of claims 46, 47, 56 and 60 under 35 U.S.C. § 112, second paragraph. The claim amendments filed 28 July 2005 also avoid the rejection of record under 35 U.S.C. § 102(e) of claims 30, 36, 40-45, 47-49, 52, 54, 55, 59, 60, 65, 72, 80-83, 92-109 and 114-119, but not the rejection of record of claim 46, over Brown et al. This communication is not made final because new objections to the specification are stated herein which require revision of the specification, new prior art is applied in rejections of claims herein under 35 U.S.C. § 102, and new grounds of rejection of claims herein are stated under 35 U.S.C. § 112, first and second paragraphs.

Objection to the Specification

The disclosure is objected to because of the following informalities:

1. The reference to preparation of oligonucleotide primers for cloning a cDNA that specifies a low-density lipoprotein (LDL) receptor at page 31, line 20, is incomplete, misleading and must be deleted. Such a deletion does not constitute new matter because it does not corroborate any other material aspect of the disclosure. Unlike the disclosures of oligonucleotide primers for cloning five target cDNAs made at page 31, lines 14-20, no LDL receptor cDNA-specific primers are disclosed, either at page 31, in Figures 13-17, or in the sequence listing. Neither is there any disclosure of detection in of LDL receptor-specific mRNA Northern blots using an LDL receptor cDNA.

2. An additional, redundant, reference is made at line 6 of page 39 to "Lys^{137}", which redundancy may be deleted. Appropriate correction is required.

Requirement for Sequence Rules Compliance in the Specification and Claims

1. Applicant's Amendment filed 28 July 2005 replaces the Sequence Disclosure filed 5 November 2004 with the original Sequence Disclosure filed on 18 October 2001. The specification does not, however, comply with 37 CFR § 1.821 because (1) several amino acid sequences which should be set forth in the Sequence Listing are not present therein, (2) two sequences, SEQ IDs NOs:14 and 46 are identical, thus the latter is redundant, and (3) 37 CFR § 1.821 requires that sequence identifiers accompany the descriptions of defined nucleotide and amino acid sequences where they are occur in the text of the specification. e.g., a designation properly stated as **"SEQ ID NO:n"** where "n" is an integer. See 37 CFR §§ 1.821(b), (c) and (d). The following list indicates the locations in the specification of (i) amino acid sequences not present in the sequence listing and (ii) amino acid sequences and nucleotide sequences that, while present in the Sequence Listing, are unaccompanied by a sequence identifier:

Unrepresented and unaccompanied by a designation:

- page 9, line 19 (this peptide is not represented in the Sequence Listing);
- page 19, line 29 (this peptide, identical to that at page 9, line 19, is not represented in the Sequence Listing);

- page 22, lines 31 and 34 (neither peptide is currently represented in the Sequence Listing);
- page 24, line 29 (this peptide, a portion of SEQID NO:37, is not separately represented in the Sequence Listing);
- page 25, lines 3-5 and 33 (none of these five peptides are currently in the Sequence Listing);
- page 32, line 19 (this trisdecapeptide is not currently in the Sequence Listing);
- page 38, lines 8, 11 and 32 (these peptides, all portions of SEQ ID NO:6, are not separately represented in the Sequence Listing);
- page 43, line 8 (this peptide portion of SEQ ID NO:6 first shown at page 38, line 8, is not separately represented in the Sequence Listing);
- page 44, line 5 (this portion of SEQ ID NO:39 is not separately represented in the Sequence Listing) and 25 (this portion of SEQ ID NO:45 is not separately represented in the Sequence Listing); and,
- page 52, lines 28 and 30 (these portions of SEQ IDs NOs:39 and 45 are not separately represented in the Sequence Listing).

Note that each unique sequence, whether part of another sequence or not, need be set forth once in the Sequence Listing.

Represented but unaccompanied by a designation:

- ▲ page 4, lines 29 (SEQ ID NO:13) and 34 (SEQ ID NO:14);
- ▲ page 8, line 13 (SEQ ID NO:13);
- ▲ page 16, lines 28 and 29 (respectively SEQ IDs NOs: 15 and 16);
- ▲ page 19, lines 6 and 7 (respectively SEQ IDs NOs:17 and 18);
- ▲ page 30 lines 26 and 27 (respectively SEQ IDs NOs: 19 and 20);
- ▲ page 31, lines 14-20 (the ten oligonucleotides of SEQ IDs NOs:21-30);
- ▲ page 32, lines 9 and 10, (SEQ IDs NOs:31 and 32), 16 and 18 (respectively SEQ IDs NOs:33 and 34);
- ▲ page 33, lines 3-6 (oligonucleotides, respectively SEQ IDs NOs:19, 35, 20, and 36);
- ▲ page 34, line 23, through page 35, line 1 (peptides of SEQ IDs NOs:37-47);
- ▲ page 39, lines 20 (SEQ ID NO:39), 29 (SEQ ID NO:44), 31 and 34 (both SEQ ID NO:45);
- ▲ page 40, lines 4-6 (SEQ IDs NOs:39 and 45(twice)), 33 and 34 (SEQ IDs NOs: 37 and 38);
- ▲ page 44, lines 7, 8, 10, 11, 15, 17 (each of which is SEQ ID NO:45);
- ▲ page 45, line 12 (SEQ ID NO:45);
- ▲ page 46, lines 24-25 (SEQ ID NO:47);
- ▲ page 47, lines 10-29 comprising Table II-A (consecutively SEQ IDs NOs:37-47);

- page 51, Table VI comprising the sequences of SEQ IDs NOs:48-71;
- page 53, lines 8, 10, 12, 14, 16, 18, 20, 22, 24-25, and 27 (in order, SEQ IDs NOs:42, 39, 40, 72, 43-45, 37, 38, and 73); and,
- page 54, lines 11, 14, 17, 20, and 23 (in order, SEQ IDs NOs:46, 47, and 74-76).

Where a sequence identifier is already present in the Sequence Listing, the appropriate sequence identifier should be stated, in parentheses, after each peptide and oligonucleotide sequence and, where no sequence identifier is present in the Sequence Listing, it should be provided as part of a revised Sequence Listing including, e.g., sequence identifiers for sequences at pages 9 and 19, 22, 24, 25, 32, 38, 43, 44 and 52, in order to bring the disclosure into compliance with 37 CFR § 1.821, which is required in response to this Office action.

2. Claims 30-32, 45, 51, 59, 60, 65, and 67 are objected to because they lack designations describing their subject matters, specifically each of the recitations "SKI-1", according to the requirements of 37 CFR § 1.821 for a Sequence Disclosure. Even if the sequences were set forth in the claims, recitations of a nucleotide or amino acid sequence positions must also include a statement of the designation, **"SEQ ID NO:n"**, where "n" is an integer corresponding to the Sequence Disclosure. See 37 CFR §§ 1.821(b), (c) and (d). Claim 30 is may be amended to avoid this objection by replacing the phrase, "a subtilisin-kexin isoenzyme (SKI-1), the amino acid sequence of which", with the phrase "the subtilisin-kexin isoenzyme SKI-1 set forth in SEQ ID NO:6, wherein the soluble polypeptide". A similar amendment to claim 31 will avoid this objection with regard to that claim, but claim 32 is best amended to avoid this rejection by specifying the intended amino acid positions of SEQ ID NO:6 after the term "SKI-1". In the case of claim 45, this objection may be avoided by amending the claim to replace both the phrase in the preamble, "a fragment of SKI-1 enzyme", and the phrase in the terminal clause, "said fragment of SKI-1", with the phrase: "the soluble polypeptide of claim 30". Claims 59 and 60 may be amended to avoid this objection both by (i) replacing the phrase, "a subtilisin-kexin isoenzyme (SKI-1)" in both preambles, and (ii) replacing the

phrases in their first clauses, respectively, "the SKI-1" and "SKI-1 activity", with the same recitation, "a polypeptide having the proteolytic activity of the SKI-1 protease having amino acid sequence set forth in SEQ ID NO:6". Simply deleting the superfluous phrase "of a SKI-1" from the dependent claims 65 and 67 will avoid this rejection with respect to these claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 45-49, 51, 52, 54, and 55 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

1. Claims 46-49 are rejected because the specification neither exemplifies nor describes the preparation of the diverse "catalytic parts" of an SKI-1 convertase of clauses (a)(2) of claims 46 and 47, required for methods of claims 46-49. Instead, it describes the preparation of a single, soluble, mature SKI-1 convertase: the truncated convertase that is described by the originally filed claim 1, the current claim 30, and by clauses (a)(1) of claims 46 and 47. The specification discloses no other species of soluble SKI-1 convertase and suggest no other species of soluble SKI-1 convertases that might represent an adequate number of species populating a genus of "fragments" that are "catalytic parts" of the amino acid sequence of SEQ ID NO:6. Deleting clauses (b) of claims 46 and 47 will overcome this rejection as it applies to claims 46-49.

2. Claims 51, 52, 54, and 55 are rejected because the specification does not exemplify, describe, or discuss preparation of peptides of having a range of "between 7 and 13 amino acids". The Remarks at page 14 of the amendment of 25 January 2005 identify no statement in the specification disclosing a range of "between 7 and 13" and a

review of pages 40-46, 53-55, and Table II-A of the specification does not suggest that a maximum length of 13 amino acids was contemplated in preparing these SKI-1 peptide substrates between 9 and 27 amino acids in length. Absent a showing of support in the specification for an upper limit or 13, the rejection of claims 51-55 may be overcome by amending claim 51 to recite, e.g., "a peptide **comprising** an amino acid sequence set forth . . . which is capable of binding to, and being cleaved by, a SKI-1 protease", where amino acid sequences defined by SEQ IDs NOs:7-12 recited in claims 51 and 52 conform to the specification's disclosure of preferred recognition sequences for SKI-1 convertase cleavage and the term "comprising" would not exclude peptides of 13 amino acids.

Claims 93-97, 99-103, 105-109 and 115-119 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

1. Claims 93, 99, 105, and 115 are rejected because the specification nowhere describes the preparation of a polypeptide of claim 93 consisting of the amino acid sequence of SEQ ID NO:6 from position 1 through position 197, preparation of a polynucleotide of claim 99 encoding the polypeptide, preparation of compositions of claim 105 comprising the polypeptide, or preparation of a vector of claim 115. Unlike the verbatim disclosures of the subject matters of claims 92, 98, 104 and 114 at page 30, lines 25-29, the specification discloses no SKI-1 polypeptide consisting of the amino acid sequence from position 1 through position 197 of SEQ ID NO:6. This rejection is best overcome by deleting claims 93, 99, 105, and 115.

2. Claims 94, 100, 106, and 116 are rejected because specification nowhere describes the preparation of a polypeptide of claim 94 consisting of the amino acid sequence from position 1 through position 169 of SEQ ID NO:6, preparation of a polynucleotide of claim 100 encoding the polypeptide, preparation of compositions of

claim 106 comprising the polypeptide, or preparation of a vector of claim 116. Unlike the verbatim disclosures of the subject matters of claims 92, 98, 104 and 114 at page 30, lines 25-29, the specification discloses no SKI-1 polypeptide consisting of the amino acid sequence from position 1 through position 169 of SEQ ID NO:6. This rejection is best overcome by deleting claims 94, 100, 106, and 116.

3. Claims 95, 101, 107, and 117 are rejected because the specification does not describe preparation of a polypeptide of claim 95 consisting of the amino acid sequence from position 17 through position 188 of SEQ ID NO:6, preparation of a polynucleotide of claim 101 encoding the polypeptide, preparation of a composition of claim 107 comprising the polypeptide, or preparation of a vector of claim 117. Instead, the specification teaches the preparation of a polynucleotide encoding a polypeptide that terminates at position 188 of SEQ ID NO:6 and that commences at an amino acid of SEQ ID NO:6 defined by the sense PCR primer at line 3 of page 33 which does not appear to provide for a glycine codon before the codon for lysine at position 18 of SEQ ID NO:6. This rejection as it applies to claims 95, 101, 107, and 117 is best overcome by amending claim 95 to describe a product by process wherein the process utilizes the sense PCR primer disclosed at line 3 of page 33 of the specification.

4. Claims 96, 102, 108, and 118 are rejected because the specification does not describe preparation of a polypeptide of claim 96 consisting of the amino acid sequence from position 17 through position 197 of SEQ ID NO:6, preparation of a polynucleotide of claim 102 encoding the polypeptide, preparation of a composition of claim 108 comprising the polypeptide, or preparation of a vector of claim 118. Instead, the specification teaches the preparation of a polynucleotide encoding a polypeptide that terminates at position 197 of SEQ ID NO:6 and that commences at an amino acid of SEQ ID NO:6 defined by the sense PCR primer at line 3 of page 33 which does not appear to provide for a glycine codon before the codon for lysine at position 18 of SEQ

ID NO:6. This rejection as it applies to claims 96, 102, 108, and 118 is best overcome by amending claim 96 to describe a product by process wherein the process utilizes the sense PCR primer disclosed at line 3 of page 33 of the specification.

5. Claims 97, 103, 109, and 119 are rejected because the specification does not describe preparation of a polypeptide of claim 97 consisting of the amino acid sequence from position 17 through position 169 of SEQ ID NO:6, preparation of a polynucleotide of claim 103 encoding the polypeptide, preparation of compositions of claim 109 comprising the polypeptide, or preparation of a vector of claim 119. Instead, the specification teaches the preparation of a polynucleotide encoding a polypeptide that terminates at position 169 of SEQ ID NO:6 and that commences at an amino acid of SEQ ID NO:6 defined by the sense PCR primer at line 3 of page 33 which does not appear to provide for a glycine codon before the codon for lysine at position 18 of SEQ ID NO:6. This rejection as it applies to claims 97, 103, 109, and 119 is best overcome by amending claim 97 to describe a product by process wherein the process utilizes the sense PCR primer disclosed at line 3 of page 33 of the specification.

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32, 45-49, 59, 60, 65 and 67 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 32 is indefinite in reciting "the soluble fragment of SKI-1" at line 4 because this phrase cannot define any particular soluble fragment, or set of soluble fragments, of a SKI-1 convertase by, e.g., structural characteristics. No preceding claim provides an antecedent basis for "the soluble fragment" and the phrase at line of claim 32 fails to define any further characteristic of the polypeptide of claim 31. While line 4 of claim 32 may be amended to overcome this rejection by describing a particular soluble SKI-1 convertase, e.g., the polypeptide of claim 30, care must be taken to determine whether

a claim 32 so amended is intended to further define the polypeptide of claim 31 or to instead describe a complex comprising that polypeptide and a particular soluble, proteolytically active SKI1 polypeptide in order to provide a proper antecedent basis for clause (a)(3) of claims 46 and 47 as discussed below.

2. Claim 45 is indefinite in reciting "a fragment of SKI-1 enzyme" because this states no identifying characteristic that would permit the artisan and the public seeking to ascertain the metes and bounds of the intended subject matter to distinguish an intended "fragment" from a free amino acid, or a dipeptide or tripeptide, that might be recovered from an "expression-supportive culture medium". Since the claim is intended to describe a recombinant method of making the soluble, proteolytically active, SKI-1 polypeptide encoded by the nucleic acid of claim 36, adopting the amendment suggested above in the objection to the claims for lack of compliance with the Sequence Rules will overcome this aspect of the rejection.

3. Claims 46-49 are indefinite because claims 46 and 47 both recite, "a complex as defined in claim 32", yet claim 32 now further defines the polypeptide of claim 31, not a complex, i.e., the polypeptide of claim 32 consists of the sequence of amino acids described in claim 31, has a relative mass of 14 kDa, and is capable of forming a complex. The specification does provide a basis for a claim properly drawn to such a complex, as well as a method of use of a complex, (i) at page 42, lines 23-27, indicating that the 14 kDa polypeptide of claims 31 and 32 is non-inhibitory and (ii) at pages 43, 45, and 46, indicating that the 14 kDa polypeptide of claims 31 and 32 is associated in a proteolytically active complex with a mature SKI-1 in the trans-Golgi network. Claims 48 and 49 are included in this rejection because they depend from claim 47 but do not resolve its ambiguity. This rejection of claims 46-49 may be overcome either by amending clause (a)(3) of claims 45 and 46 to delete the reference to claim 32 and to instead separately describe a complex disclosed in the specification of the polypeptide

of claim 31 and a mature SKI-1 convertase or by amending claim 32 to make it an independent claim describing a complex formed by the polypeptide of claim 31 and a mature SKI-1 convertase.

4. Claim 48 is independently indefinite in reciting, "in the presence of a cellular population", because it is not clear what conditions are intended, or required, by the term "presence", providing no identifying characteristic that would permit the artisan and the public seeking to ascertain the metes and bounds of the intended subject matter to determine whether the method for producing a protein is accomplished outside the cell wherein a SKI-1 convertase or SKI-1-comprising complex is expressed or accomplished due to the contributions of factors or conditions emanating from cells not expressing a SKI-1 convertase or SKI-1-comprising complex the presence of which is nonetheless required. The phrase is not clear enough to determine whether or not there is a disclosure in the specification of either a contributing or a non-contributing "cellular population" in a claimed method to suggest an amendatory remedy other than deleting the phrase.

5. Claims 59 and 60 are indefinite because the claims are ambiguous in failing to specify what is intended by the phrases, "the activity of a subtilisin-kexin isoenzyme (SKI-1)", and, "has (having) SKI-1 activity". Amending both claims to insert "proteolytic" before each occurrence of "activity" will overcome this aspect of the rejection.

6. Claims 65 and 67 are indefinite in reciting "polypeptide of **a** SKI-1 as defined . . ." because use of the indefinite article "a" indicates a non-specific SKI-1, implying that no particular fragment is comprised by a claimed composition. This aspect of the rejection may be overcome by amending claim 65 to simply recite, "[a] composition comprising a polypeptide as defined in claim 30", and amending claim 67 to simply recite, "[a] composition comprising a polypeptide as defined in claim 31".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 46-49 are rejected under 35 U.S.C. § 102(e) as being anticipated by Brown et al., of record, essentially for reasons set forth in the communication of 5 May 2004.

The truncated SKI-1 convertase of claim 30 is also the SKI-1 convertase of clause (a)(1) of claims 46 and 47 and the only structural characteristic of a "catalytic part" of the SKI-1/Site-1 convertase of claim 30 is that it comprises less of the amino acid sequence of SEQ ID NO:6 than the truncated convertase of claim 30. Brown et al. specifically disclose the method of claim 46 by cleaving a SKI-1/Site-1 convertase substrate, which is their SEQ ID NO:13 that is not part of a sterol-regulatory element binding protein, with a truncated, mature, SKI-1/Site-1 convertase that is a "catalytic part" of the SKI-1/Site-1 convertase of claim 30 in that it has the amino acid sequence from position 187 through position 983 of SEQ ID NO:6 herein, resulting in cleavage of the substrate upon contact with their truncated SKI-1/Site-1 convertase. See columns 63-68 and Table 3.

Brown et al. inherently disclose the methods of claims 47-49 by recombinantly producing a protein from a precursor which is a SKI-1/Site-1 convertase substrate in a host cell transfected with a nucleic acid encoding a "catalytic part" of a SKI-1/Site-1 convertase of the SKI-1/Site-1 convertase of claim 30 wherein a SKI-1 convertase is itself the precursor and the cleaved and recovered product. Specifically, Brown et al. express a precursor form of their truncated SKI-1/Site-1 convertase having a carboxyl terminus at position 983, that cleaves a propeptide region from the precursor, truncated,

SKI-1/Site-1 convertase having a carboxyl terminus at position 983 in order to recover the mature, truncated, SKI-1/Site-1 convertase. See columns 63-68.

Claims 51 and 52 are rejected under 35 U.S.C. § 102(b) as being anticipated by Dowdie, EP 0 218 479.

Dowdie discloses the preparation of dodecapeptides from several sources wherein the three disclosed at page 15, lines 37, 43 and 45, all have the amino acid sequence,

Arg – Ser – **Ala** – **Phe** – Ile – Pro – **Asp** – **Asp** – **Asp** – Lys – Val – Arg,

a sequence that anticipates claims 51 and 52 herein by meeting structural limitations of SEQ IDS NOs: 7-12 herein.

Claims 51, 52, 54 and 55 are rejected under 35 U.S.C. § 102(b) as being anticipated by Habets et al., WO 93/13127.

Habets et al. disclose the preparation of a dodecapeptide which is their SEQ ID NO:7 and is also set forth at page 2, lines 1-9, having the amino acid sequence,

NH_3 – Asp – **Arg** – Glu – **Val** – **Leu** – Tyr – Arg – **Glu** – Phe – **Asp** – **Glu** – Met – OH,

a sequence that anticipates claims 51 and 52 herein by meeting structural limitations of SEQ IDS NOs: 7, 8, 11 and 12 herein. Habets et al. further anticipate claims 54 and 55 in their disclosure at page 8, lines 22-37, of a reagent comprising the peptide and a "labeling substance" that may be a fluorescent compound.

Conclusion

Claims 30, 31, 36, 37, 40-44, 72, 73, 80-83, 92, 98, 104 and 114 are allowed, essentially for the reasons set forth at pages 7 and 8 of the communication mailed 26 January 2005. Claims 53 and 56 describe subject matter free of the prior art of record but are objected to because they depend from the rejected claim 51 and would be allowable if rewritten in independent form.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you

have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Dr. Kathleen Kerr, can be reached at 571.272.0931. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

William W. Moore
14 October 2005

NASHAAT T. NASHED PHD.
PRIMARY EXAMINER

Continuation of Disposition of Claims: Claims pending in the application are 30-32,36,37,40-49,51-56,59,60,65,67,72,73,80-83,92-109 and 114-119.